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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,701	01/14/2002	Klaus Ducker	MERCK 2354	8622

23599 7590 05/17/2004

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,701	DUCKER ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08222002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comaprison A,B*.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-9 in the response filed 3/24/2004 is acknowledged. The traversal is on the ground(s) that there would not be an undue burden on the Examiner to search all the claims. This is not found persuasive because CFR 1.475 (a) indicates that a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. CFR 1.475(e) indicates that the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim (MPEP R-90 -- R-91 and 1893.03(d)). Applicant elected the invention of Group I, Claims 1-9, drawn to nucleic acids encoding ICSR-1 and the ICSR-1 polypeptide. 37 CFR 1.475 (b) describes the combinations of categories which will be considered to have unity of invention when applications contain claims to different categories of invention. The claims of Groups II and III were not joined with claims reciting nucleic acids encoding ICSR-1 and the ICSR-1 polypeptide because the invention of Group I was found to have no special technical feature that defined the contribution over the prior art of U.S. Patent No. 5,759,804 (Godiska et al.), Therefore, the restriction set forth on 2/23/2004 is appropriate.

The requirement is still deemed proper and is therefore made FINAL.

Specification

The disclosure is objected to because of the following informalities: On pages 8-9 there are numerous uses of a phrase in German pointing out an error due to missing information.

Appropriate correction is required.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed, e.g. "The ICSR-1 GPCR and encoding polynucleotides", or something similar.

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. The claimed invention is not supported by either a specific and substantial asserted utility or a well-

established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

It is clear from the instant specification that the nucleic acid encoding the ICSR-1 polypeptide has been assigned a function because of its similarity to known proteins (Specification at 8). However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods has led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). Furthermore, Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Additionally, Yan et al. teaches that in certain cases, a change of only two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* 290: 523-527, 2000). Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein.

Such questionable interpretations are written into the sequence database and are then considered facts.

Additionally, even if, *arguendo*, the nucleic acid encoding the ICSR-1 protein is found to be a GPCR, the ligand is unknown. Since the ligand of this protein is unknown, the function of the protein is also unknown. Neither the specification nor the art of record disclose any diseases or conditions associated with the function or expression of the ICSR-1 protein, therefore, there is no "real world" context of use. Further research to identify or reasonably confirm a "real world" context of use is required. In the instant case, the fact that the claimed invention encodes a GPCR is not sufficient to establish a specific and substantial utility. Although GPCRs have been found to be involved in many different processes and have been the target of much research and drug discovery, unless the specific ligand for each GPCR is known, unless the biological activity of the GPCR is disclosed and unless the processes that each GPCR is involved in are identified, the GPCR has no "real world" use, and therefore, lacks specific and substantial utility.

The specification asserts several allegedly patentable utilities for the claimed nucleic acid encoding an ICSR-1 polynucleotide. Among the alleged utilities is the use of the polynucleotide as hybridization probes for screening libraries an assessing gene expression patterns in a gene chip format (Specification at 13). This asserted utility is not substantial and specific. Hybridization probes can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA or DNA targets. Additionally, use of the claimed polynucleotide in an array for selectivity screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. This is a utility that would

apply to virtually every member of a general class of materials, such as any collection of proteins or DNA.

Additionally, the Specification asserts that the sequence can be used to identify mutations in SEQ ID NO: 1, or inappropriately expressed ICSR-1s for the diagnosis of disease (Specification at 12). However, this asserted utility is not specific or substantial. The specification does not disclose disorders associated with a mutated, deleted, or translocated ICSR-1 gene. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Further, the specification does not disclose the tissues or cell types the polypeptide/mRNA are normally expressed in. The specification also discloses nothing about the normal levels of expression of the polypeptide/mRNA. The abnormal levels of the polypeptide/mRNA cannot be determined until a baseline control level is established.

After complete characterization, this protein may be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson,* 148 USPQ 689 (Sup. Ct., 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 USC § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a nucleic acid encoding a polypeptide, which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as ICSR-1, the instant invention is incomplete. The polypeptide encoded by the nucleic acids of the instant invention is known to be structurally analogous to proteins that are known in the art as GPCRs. In the absence of knowledge of the natural ligand or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances that inhibit its activity is clearly to use it as the object of further research that has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for ICSR-1 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

Claims 1-9 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well

established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if, *arguendo*, the nucleic acid of the instant invention is found to have a patentable utility, claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding an amino acid of SEQ ID NO: 2, or a nucleic acid with the sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for a nucleic acid which is 95% identical to SEQ ID NO: 1; or a polypeptide 95% identical to SEQ ID NO: 2; or variants and fragments of SEQ ID NO: 1; or fragments of SEQ ID NO: 1 having at least 15 or 100 nucleotides; or fragments and variants of SEQ ID NO: 2; or host cells comprising such polynucleotides; or fusion proteins comprising such polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-9 are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the characteristics of ICSR-1. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of ICSR-1. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, As an example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane

conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Additionally, Yan et al. teaches that in certain cases, a change of only two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* 290: 523-527, 2000).

Since the claims encompass variant nucleic acids and polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims as written do not set forth a

functional limitation for the polynucleotides and encoded polypeptides encompassed by the claims. Since the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides and encoded polypeptides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polynucleotides and encoded polypeptides, since the skilled artisan would have to first make polynucleotide and polypeptide variants, but there is no functional limitation set forth for the claimed encoded polypeptides. Thus, since the claims do not enable one of skill in the art to make and use the claimed polynucleotides and polypeptides, but only teaches how to screen for the claimed polynucleotides and polypeptides, and since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to a nucleic acid which is 95% identical to SEQ ID NO: 1; or a polypeptide 95% identical to SEQ ID NO: 2; or variants and fragments of SEQ ID NO: 1; or fragments of SEQ ID NO: 1 having at least 15 or 100 nucleotides; or fragments and variants of SEQ ID NO: 2; or host cells comprising such polynucleotides; or fusion proteins comprising such polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid with a sequence as set forth in SEQ ID NO: 1 and the polypeptide of SEQ ID NO: 2 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the term "stringent conditions", which is a conditional term and renders the claim indefinite. Furthermore, some nucleic acids which might hybridize under conditions of moderate stringency, for example, would fail to hybridize under conditions of high stringency. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific conditions supported by the specification which Applicant considers to be "stringent". Claim 5 is rejected insofar as it depends on the recitation in claim 4 of "stringent conditions".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-8 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,759,804 (Godiska et al.).

The '804 patent disclose the cloning and expression of several G protein coupled receptors (column 3, lines 15-30). The nucleic acid sequence which encodes the R12 GPCR is set forth in SEQ ID NO: 43, and is 11.7% identical to the instant sequence of SEQ ID NO: 1, (see Sequence Comparison A, attached). This nucleic acid anticipates claims 4-5 because it comprises sequences which are "fragments or variants" of SEQ ID NO: 1, and also contains a stretch of 15 nucleic acids which is 100% identical to SEQ ID NO: 1. Claims 6-8 are anticipated because the '804 patent discloses expression vectors and host cells comprising the polynucleotides (column 3, lines 43-65) as well as method of producing the encoded protein (column 4, lines 1-15). The '804 patent also discloses that amino acid sequence of the encoded R12 polypeptide in SEQ ID NO: 44, which is 19.7% identical to instantly claimed SEQ ID NO: 2 (see Sequence Comparison B, attached). Claim 1 is anticipated because the R12 polypeptide comprises sequences that are fragments or variants of SEQ ID NO: 2.

Claims 1, 4-9 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,639,597 (Lauffer et al.).

The claims are drawn to fragments and variants of the polynucleotide of SEQ ID NO: 1 and fragments and variants of SEQ ID NO: 2. There is no length limitation for the "fragment" and thus the fragment may be as short as 1 amino acid or 1 nucleic acid. The '597 patent discloses methods of determining the binding behavior of receptor proteins in the cell membrane (column 1, lines 15-17). Since these receptor proteins comprise single amino acids which can be considered fragments of SEQ ID NO: 2, and since the nucleic acids encoding the polypeptides

comprise single nucleotides which are fragments of SEQ ID NO: 1, claims 1, 4-8 are anticipated. The '597 patent additionally discloses fusion proteins comprising the ligand binding portion of a receptor protein and the Fc region of an immunoglobulins (column 1, lines 45-65), thus claim 9 is anticipated.

Conclusion

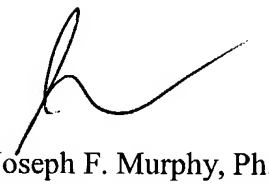
No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
May 13, 2004

Sequence Comparison A

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RESULT 8
US-08-153-848-43
; Sequence 43, Application US/08153848
; Patent No. 5759804
;  GENERAL INFORMATION:
;    APPLICANT:  Godiska, Ronald
;    APPLICANT:  Gray, Patrick W.
;    APPLICANT:  Schweikart, Vicki L.
;    TITLE OF INVENTION:  No. 5759804el Seven Transmembrane Receptors
;    NUMBER OF SEQUENCES:  64
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Marshall, O'Toole, Gerstein, Murray &
;      ADDRESSEE:  Bicknell
;      STREET:  6300 Sears Tower, 233 South Wacker Drive
;      CITY:  Chicago
;      STATE:  Illinois
;      COUNTRY:  USA
;      ZIP:  60606
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/153,848
;      FILING DATE:
;      CLASSIFICATION:  514
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 07/977,452
;      FILING DATE:  17-NOV-1992
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  No. 5759804and, Greta E.
;      REGISTRATION NUMBER:  35,302
;      REFERENCE/DOCKET NUMBER:  31794
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (312) 474-6300
;      TELEFAX:  (312) 474-0448
;      TELEX:  25-3856
;  INFORMATION FOR SEQ ID NO:  43:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  1901 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  DNA (genomic)
;    FEATURE:
;      NAME/KEY:  CDS
;      LOCATION:  701..1717
US-08-153-848-43

  Query Match             11.7%;  Score 130.8;  DB 1;  Length 1901;
  Best Local Similarity   50.9%;  Pred. No. 1.5e-15;
  Matches  436;  Conservative    0;  Mismatches  387;  Indels   33;  Gaps    4;

Qy        117 CAACGCGCTAGCCCTCTGGGTCTTCCTGCGCGCGCTGCGCGTGCACTCGGTGGTGAGCGT 176
              |||  | || || || ||| | ||| | || |  |             |   ||  | |||
Db        844 CAATACCCTGGCTCTGTGGCTTTTCATCCGAGACCACAAGTCCGGGACCCCGGCCAACGT 903

Qy        177 GTACATGTGTAACCTGGCGGCCAGCGACCTGCTCTTCACCCTCTCGCTGCCCGTTCGTC- 235
              || | ||    | ||||| |    |||| ||   | |   ||    ||||||   || |
Db        904 GTTCCTGATGCATCTGGCCGTGGCCGACTTGTCGTGCGTGCTGGTCCTGCCCACCCGCCT 963

Qy        236 --TCTCCTACTACGCACTGCACCACTGGCCCTTCCCCGACCTCCTGTGCCAGACGACGGG 293
                ||| | ||| | |   | ||||||||| ||    ||  ||   ||||     || ||
Db        964 GGTCTACCACTTCTCTGGGAACCACTGGCCATTTGGGGAAATCGCATGCCGTCTCACCGG 1023

Qy        294 CGCCATCTTCCAGATGAACATGTACGGCAGCTGCATCTTCCTGATGCTCATCAACGTGGA 353
              |  | ||||| |  | |||||||||| ||||  |  ||||||  |    ||||| ||  ||
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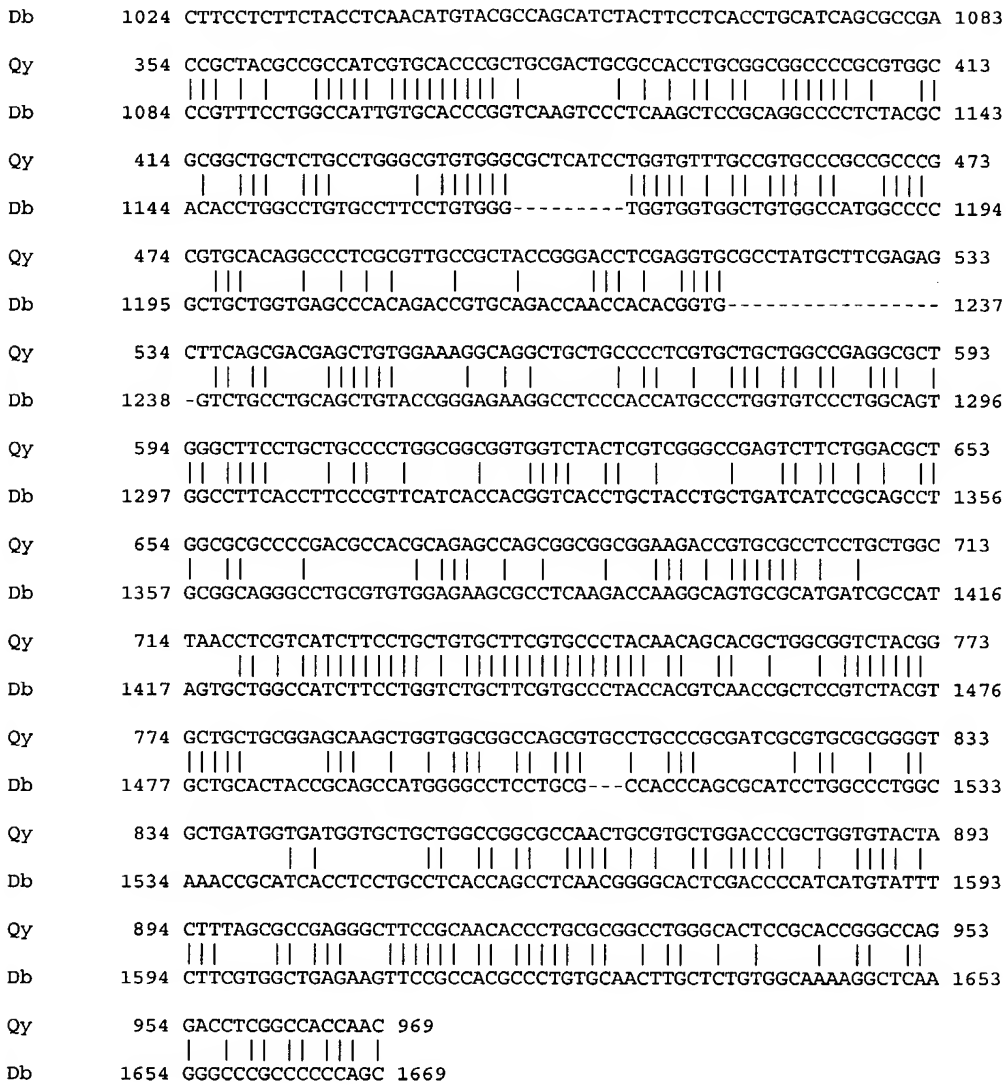
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Db 1195 GCTGCTGGTGAGCCCACAGACCGTGCAGACCAACCACACGGTG---------- 1237
Qy 534 CTTCAGCGACGAGCTGTGGAAAGGCAGGCTGCTGCCCCTCGTGCTGCTGGCCGAGGCGCT 593
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Db 1297 GGCCTTCACCTTCCCGTTCATCACCACGGTCACCTGCTACCTGCTGATCATCCGCAGCCT 1356
Qy 654 GGCGCGCCCCGACGCCACGCAGAGCCAGCGGCGGCGGAAGACCGTGCGCCTCCTGCTGGC 713
Db 1357 GCGGCAGGGCCTGCGTGTGGAGAAGCGCCTCAAGACCAAGGCAGTGCGCATGATCGCCAT 1416
Qy 714 TAACCTCGTCATCTTCCTGCTGTGCTTCGTGCCCTACAACAGCACGCTGGCGGTCTACGG 773
Db 1417 AGTGCTGGCCATCTTCCTGGTCTGCTTCGTGCCCTACCACGTCAACCGCTCCGTCTACGT 1476
Qy 774 GCTGCTGCGGAGCAAGCTGGTGGCGGCCAGCGTGCCTGCCCGCGATCGCGTGCGCGGGGT 833
Db 1477 GCTGCACTACCGCAGCCATGGGGCCTCCTGCG---CCACCCAGCGCATCCTGGCCCTGGC 1533
Qy 834 GCTGATGGTGATGGTGCTGCTGGCCGGCGCCAACTGCGTGCTGGACCCGCTGGTGTACTA 893
Db 1534 AAACCGCATCACCTCCTGCCTCACCAGCCTCAACGGGGCACTCGACCCCATCATGTATTT 1593
Qy 894 CTTTAGCGCCGAGGGCTTCCGCAACACCCTGCGCGGCCTGGGCACTCCGCACCGGGCCAG 953
Db 1594 CTTCGTGGCTGAGAAGTTCCGCCACGCCCTGTGCAACTTGCTCTGTGGCAAAAGGCTCAA 1653
Qy 954 GACCTCGGCCACCAAC 969
Db 1654 GGGCCCGCCCCCCAGC 1669

Sequence Comparison B

```
RESULT 13
US-08-153-848-44
; Sequence 44, Application US/08153848
; Patent No. 5759804
;  GENERAL INFORMATION:
;    APPLICANT:  Godiska, Ronald
;    APPLICANT:  Gray, Patrick W.
;    APPLICANT:  Schweikart, Vicki L.
;    TITLE OF INVENTION:  No. 5759804el Seven Transmembrane Receptors
;    NUMBER OF SEQUENCES:  64
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Marshall, O'Toole, Gerstein, Murray &
;      ADDRESSEE:  Bicknell
;      STREET:  6300 Sears Tower, 233 South Wacker Drive
;      CITY:  Chicago
;      STATE:  Illinois
;      COUNTRY:  USA
;      ZIP:  60606
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/153,848
;      FILING DATE:
;      CLASSIFICATION:  514
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 07/977,452
;      FILING DATE:  17-NOV-1992
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  No. 5759804and, Greta E.
;      REGISTRATION NUMBER:  35,302
;      REFERENCE/DOCKET NUMBER:  31794
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (312) 474-6300
;      TELEFAX:  (312) 474-0448
;      TELEX:  25-3856
;  INFORMATION FOR SEQ ID NO:  44:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  339 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-153-848-44

  Query Match             19.7%;  Score 374.5;  DB 1;  Length 339;
  Best Local Similarity   32.7%;  Pred. No. 1.3e-21;
  Matches   93;  Conservative   53;  Mismatches  127;  Indels   11;  Gaps    4;

Qy         29 YSLVLAAGLPLNALALWVFLRALRVHSVVSVYMCNLAASDLLFTLSLPVRLSY-YALHHW 87
              | |      |  | ||||:|:|  :  :  :|:: :|| :||    | || || | :: :||
Db         38 YLLDFILALVGNTLALWLFIRDHKSGTPANVFLMHLAVADLSCVLVLPTRLVYHFSGNHW 97

Qy         88 PFPDLLCQTTGAIFQMNMYGSCIFLMLINVDRYAAIVHPLRLRHLRRPRVARLLCLGVWA 147
              || :: |: || :| :||| |  ||  |: ||: |||||::   ||||  | | |  :|
Db         98 PFGEIACRLTGFLFYLNMYASIYFLTCISADRFLAIVHPVKSLKLRRPLYAHLACAFLWV 157

Qy        148 LILVFAVPAARVHRPSRCRYRDLEVRLCFESFSDELWKGRLLPLVLLAEALGFLLPLAAV 207
              :: |   |   :  |   :     | |       :|:: :     |:: |: |  |
Db        158 VVAVAMAPL--LVSPQTVQTNHTVVCL-------QLYREKASHHALVSLAVAFTFPFITT 208

Qy        208 VYSSGRVFWTLARPDATQSQRRRKTVRLLLANLVIFLLCFVPYNSTLAVYGLLRSKLVAA 267
              |     :  :| :    : : : | ||::   | |||:|||||:   :|| :|  :   |
Db        209 VTCYLLIIRSLRQGLRVEKRLKTKAVRMIAIVLAIFLVCFVPYHVNRSVY-VLHYRSHGA 267

Qy        268 SVPARDRVRGVLMVMVLLAGANCVLDPLVYYFSAEGFRNTLRGL 311
              |   :  :     :   |   |  |||::|:| || ||: |  |
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Db 268 SCATQRILALANRITSCLTSLNGALDPIMYFFVAEKFRHALCNL 311